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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,621	12/11/2003	Atul Varadhachary	HO-P02705US2	8531

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 01/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,621	VARADHACHARY ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *23-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/11/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/11/04;7/29/04;* 12/8/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-22 and 33-34 in the response filed November 17, 2004 is acknowledged. Therefore, claims 1-22 and 33-34 are examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 10 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claim 10 is indefinite because the claim recites the term "said N-terminal lactoferrin variant comprises at least 1% to at least 50% of the lactoferrin composition", while claim 8, from which claim 10 depends from, cites "said lactoferrin composition comprises an N-terminal lactoferrin variant", it is not clear how the N-terminal lactoferrin variant, which is a peptide, can comprise a portion (1-50%) of the lactoferrin composition, and whether the percentage is "weight by volume" or "weight by weight"?

4. Claim 22 is indefinite as being dependent from claim 21, which cites the lactoferrin enhances the activity of cytokine, while TNF-α is a known pro-inflammatory cytokine and lactoferrin inhibits its activity (see page 7, lines 1-7 of the specification).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

5. Claims 1-6, 11-15, 18-22 and 34 are rejected under 35 U.S.C. 102(b) as anticipated by Ando *et al.* (U. S. Patent 5,576,299, published November 19, 1996).

Ando *et al.* disclose a formulation containing lactoferrin or transferrin is used for treating opportunistic infectious diseases under immunodeficient condition caused by Lentiviral infection (column 2, lines 10-21), e.g., granules containing human apolactoferrin (350 mg/day; claims 18 and 19) were given to HIV positive patients with recurrent stomatitis and gingivitis once daily for 4 weeks, and the inflammation in the oral cavity and pain was ameliorated after the treatment (Example 2; claims 1-3, 5, 6, 11 and 34); and feline immunodecificiency virus (FIV)-positive cats were treated with bovine native lactoferrin (20 mg/kg daily), which was dissolved in distilled water (claim 4), the solution was sprayed over ulcers and aphthae in the oral cavity (claim 13), the treatment lasted 7 days to several months, and the appetite increased and the pain ameliorated after the lactoferrin treatment (Example 4). The reference also teaches the

pharmaceutical composition may contain the active compound (i.e., transferrin/lactoferrin) together with a solid or liquid pharmaceutically acceptable carrier, and the formulation may be administered orally, topically or intravenously (claim 12); suitable excipients such as sugar, gelatin, magnesium carbonate or magnesium stearate (a known antacid; claim 14) may be employed; and the composition can be in sustained-release formulations (column 4, line 21-column 5, line 3; claim 15). Although Ando *et al.* do not specifically indicate lactoferrin reduces the production or activity of pro-inflammatory cytokines (e.g., TNF-α), or enhances the production or activity of certain cytokines (e.g., IL-18), the reference teaches the administration of the same lactoferrin as the claimed invention, where the lactoferrin is expected to produce these effects (claims 20-22).

6. Claims 1-7, 11-22 and 34 are rejected under 35 U.S.C. 102(e) as anticipated by Kruzel *et al.* (US 2003/0056067, filed May 7, 2002).

Kruzel *et al.* teach lactoferrin (LF) tablets containing 95.45 parts dextrose, 2.97 parts bovine LF, and 0.53 parts calcium stearate (a known antacid) was self-administered by an adult woman with a long history of rheumatoid arthritis, and pain relief was observed as soon as a regime was initiated in which two tablets of lactoferrin were taken orally each day (Examples 2 and 5; claims 1-6, 11, 14 and 34). The reference also indicates human recombinant lactoferrin may be used alone or in combination with bovine lactoferrin (paragraph [0037]; claim 7); and lactoferrin can be administered enteraly (claims 15-17), preferably orally, or parenterally, preferably intravenously (claim 12), in the form of injectable solution, or, as a liposomal formulation such as transdermal patches (claim 13), and a single or twice daily dose of 0.01 mg to 20 mg of lactoferrin per kg of body weight is administered (paragraph [0038]; claims 18 and

19). Although Kruzel *et al.* do not specifically indicates lactoferrin reduces the production or activity of pro-inflammatory cytokines (e.g., TNF-α), or enhances the production or activity of certain cytokines (e.g., IL-18), the reference teaches the administration of the same lactoferrin as the claimed invention, where the lactoferrin is expected to produce these effects (claims 20-22).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-4, 8, 9, 11-13, 15, 18-19, 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Olmarker *et al.* (WO 02/080891, October 17, 2002) in view of Hanson *et al.* (WO 00/01730, January 13, 2000).

Olmarker *et al.* teach the use of a TNF inhibitor (e.g., lactoferrin and peptides derived from lactoferrin disclosed in WO 00/01730; page 8, lines 1-3) for the production of a pharmaceutical composition for the treatment of low back pain, where the low back pain may be

the result of unknown causes (idiopathic) or may be related to various kinds of spine trauma, including whiplash injury (page 5, line 34-page 6, line 13); the pharmaceutical composition is administered parenterally, orally, or topically in a therapeutically effective amount to an improvement of the patient's condition, and may comprise an inert vehicle or pharmaceutically acceptable carriers (claims 1-4, 11-13, 33 and 34); pharmaceutical composition may be formulated as a sustained-release preparation (claim 15); and the suitable doses for different administration route are given, e.g., 0.1-25 mg, intrathecally, daily-every 3rd month (page 8, line 26- page 9, line 30; claims 18-19). However, Olmarker *et al.* do not specifically identify the peptides derived from lactoferrin being N-terminal lactoferrin variant. Hanson *et al.* teach the peptides derived from N-terminal end of lactoferrin, e.g., the peptides have 14 amino acid residues and corresponds to residues 18-31 of human lactoferrin with some alterations, e.g., C-20 is replaced by A, Q-22 is replaced by K, and N-26 is replaced by D, which have the same and better properties (page 3, lines 10-24; claims 8-9). At the time the invention was made, it would have been obvious that a person of ordinary skill in the art is motivated to use the N-terminal lactoferrin variant as taught by Hanson *et al.* to prepare a lactoferrin composition for the treatment of low back pain as indicated by Olmarker *et al.* because the new peptides resemble human lactoferrin but they are easier and cheaper to produce, and are essentially as efficient as human lactoferrin in the treatment (page 3, lines 3-9). Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

Conclusion

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CMK
January 14, 2005